

**REMARKS**

Claims 1-6, 8, 10 and 15 - 23 and 25 - 35 are pending in the application. Claim 1, 25 and 26 are currently amended. Claims 2 - 6, 8, 10, 15-23 and 25-35 were previously presented, claims 7, 9, 11-14 and 24 were canceled. A copy of the claims now pending in the application in accord with 37 CFR 1.121, as revised, has been provided.

No new matter has been introduced by virtue of the amendments made herein. Accordingly, applicants respectfully request their entry. In view of the amendments made herein and the remarks below, applicants respectfully request reconsideration and withdrawal of the rejection set forth in the August 25, 2004 office action.

**Rejection under 35 USC § 112, first paragraph**

The Examiner maintained the rejection of claims 1-6, 8, 10 and 15-35 under 35 USC § 112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected , to make and/or use the invention, for reasons of record and stated above. The Examiner cites the Wands factors and states that the additional active ingredients are not described in the disclosure in such a way the one of ordinary skill in the art would know how to prepare the various compounds suggested by claims 1-6, 8,10 and 15-35.

Applicants submit that the second paragraph of the instant specification recites: "The compounds of this invention may also be used ... in combination with muscarinic agonists in order to stimulate both central muscarinic and nicotinic receptors for the treatment, for example, of ALS, cognitive dysfunction, age related cognitive decline; AD, PD, stroke, Huntington's Chorea and TBI; in combination with neurotrophic factors such as NGF in order to maximize cholinergic enhancement for the treatment, for example, of ALS, cognitive dysfunction, age related cognitive decline, AD, PD stroke, Huntington's Chorea and TBI; or in combination with agents that slow or arrest AD such as cognition enhancers, amyloid aggregation inhibitors, secretase inhibitors, tau kinase inhibitors, neuronal antiinflammatory agents and estrogen-like therapy." Applicants submit that the functional definition of the aforementioned agents recited in the instant specification along with the disclosure of the instant specification provides adequate guidance to one of ordinary skill in the art to enable making and using the instant pharmaceutical compositions as recited in the claims. Applicants further submit that it is well known in the art that numerous publications and articles pertain to the use of specific muscarinic agonists, neurotrophic factors, cognition enhancers, amyloid aggregation inhibitors, secretase inhibitors, tau kinase inhibitors, neuronal antiinflammatory agents and estrogen-like agents for the treatment of disorders and diseases such as Alzheimer's disease (AD). It is common practice in the art to refer to such agents functionally e.g. "muscarinic agonists" as is done in the instant

specification. The individual of ordinary skill in the art can easily identify specific members of any of the aforementioned classes and formulate them with the active ingredient of instant formula I using principles and procedures that are common knowledge in the art, the guidance provided by the instant specification and readily available publications. Applicants have appended abstracts and articles which report on the use of the classes of agents recited in the instant specification and claims in the treatments of disorders such as AD. These include: "Muscarinic agonists and antagonists in the treatment of Alzheimer's disease", W. Greenlee, et al, *// Farmaco* vol. 56, #4, April 1, 2001, pp247-250; "Therapeutic Strategies in Alzheimer's Disease: "M1 Muscarinic Agonists", A. Fisher, *Jpn. J. Pharmacol.* Vol. 84, 101-112 (2000); "β-Amyloid Aggregation Inhibitors for the Treatment of Alzheimer's Disease: Dream or Reality?", P. Talaga, *Mini Reviews in medicinal Chemistry*, Vol.1, 175-186 (2001); "Muscarinic agonists- a logical approach for AD?", A. Korczyn, *Alzheimer Insights Online*, vol. 7, No. 4 (see References), a catalog entry for commercially available secretase inhibitors which provides references (see references 2-5) on a specific secretase inhibitor and an abstract of the article "Limited efficacy of pentoxyfylline as anti-inflammatory agent in experimental pneumococcal meningitis, G. Zysk, et al., *Clin Exp Immunol.*, Vol. 107(3), 458-461 (1997). In addition, applicants submit that the Examiner has earlier conceded that the specification is "enabling for the pharmaceutical compositions of the compounds of formula I...." For the foregoing reasons, applicants respectfully submit the specification is enabling to those skilled in the art seeking to formulate the compounds of formula I into the pharmaceutical compositions that include the classes of active ingredients recited in claim 1. Applicants submit that claims 1-6, 8, 10 and 15-23 and 25-35 are patentable under 35 USC § 112, first paragraph, and respectfully request the Examiner to withdraw the rejection.

The applicants acknowledge the Examiner's withdrawal of the rejection of claims 15 and 16 under 35 USC § 112, first paragraph, and the withdrawal of rejections under 35 USC § 112, second paragraph, labeled paragraph 4), of the office action of August 25, 2004.

**Rejection Under The Judicially Created Doctrine Of Obviousness-Type Double Patenting**

The Examiner provisionally rejected claims 1-6, 8, 10, 15-19, 22, 24-27 and 30-35 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-34 of copending Application No. 10/348,381. The Examiner asserts that the analgesic agents of 10/348,381 includes agents whose activity overlaps with the agents recited in the instant claims. The Examiner cites the example of COX 2 inhibitors "known to be anti-inflammatory agents. Applicants submit that the aforesaid rejection is provisional, pending the disposition of the status of the allegedly conflicting claims of copending Application No. 10/348,381. Applicants therefore request that the instant provisional rejection be held in abeyance until the status of the claims of Application No. 10/348,381 is clarified. In addition,

applicants request that the instant rejection be held in abeyance until the instant claims are found to be otherwise allowable.

Claims 1-6, 8, 10, 15-19, 22, 24-28 and 30-35 were also provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-18 of copending Application No. 10/348,399. The Examiner asserts that the anxiolytic agents of claims 1-18 of 10/348,399 can also be considered a muscarinic agonist or a neurotrophic factor. Applicants submit that the aforesaid rejection is provisional, pending the disposition of the status of the allegedly conflicting claims of copending Application No. 10/348,399. Applicants therefore request that the instant provisional rejection be held in abeyance until the status of the claims of Application No. 10/348,399 is clarified. In addition, applicants request that the instant rejection be held in abeyance until the instant claims are found to be otherwise allowable.

The applicants acknowledge the Examiner's withdrawal of the provisional obviousness-type double patenting rejection of claims 1, 3-6, 8, 10, and 15-26 over claims 7-10 of copending Application No. 10/075,843 in paragraph 7 of the office action of August 25, 2004.

The applicants acknowledge the Examiner's withdrawal of the obviousness-type double patenting rejection of claims 1, 3, 8, 10 and 24-26 over claims 1-3 of US Patent 6,605,610 in paragraph 8 of the office action of August 25, 2004.

The applicants acknowledge the Examiner's withdrawal of the obviousness-type double patenting rejection of claims 1-6, 8, 10 and 24-35 over claims 12-14 of US Patent 6,410,550 in paragraph 9 of the office action of August 25, 2004.

#### **Rejection under 35 USC § 112, second paragraph**

The Examiner cited the following new grounds for rejection of claims 1, 8, 10 and 15-35 under 35 USC § 112, second paragraph:

a) Use of the phrases "monocyclic and bicyclic rings may optionally be substituted with one or more substituents" and "preferably from zero to two substituents". Without prejudice and in the interests of facilitating prosecution, applicants have amended claim 1 by deletion of the phrase "preferably from zero to two substituents for the monocyclic rings and from zero to three substituents for the bicyclic rings."

b) Alleged insufficient antecedent basis for "2-fluorobenzamide" in the first species of claim 15 which depends on claim 1. Without prejudice and in the interests of facilitating prosecution, applicants have amended claim 1 by addition of the language: "with the proviso that when R<sup>1</sup> is hydrogen and R<sup>2</sup> is 4-hydroxy, then R<sup>3</sup> is 5-(2-fluorobenzamidyl)." Support for this proviso may be found at Example 30 of the instant specification. Applicants submit sufficient antecedent basis has thereby been provided.

c) Alleged insufficient antecedent basis for the recital of "acetamide" in the fourth species of claim 16. Applicants respectfully traverse. Claim 1 recites that formula 1 may have R<sup>1</sup> = H, R<sup>2</sup> = H and R<sup>3</sup> = -CONR<sup>5</sup>R<sup>6</sup> wherein R<sup>5</sup> may be H and R<sup>6</sup> may be C<sub>1</sub> alkyl which corresponds to the compound N<sup>1</sup>-[10-azatricyclo[6.3.1.0<sup>2,7</sup>]dodeca-2(7),3,5-trien-4-yl]acetamide. Applicants submit the fourth species of claim 4 therefore has sufficient antecedent basis.

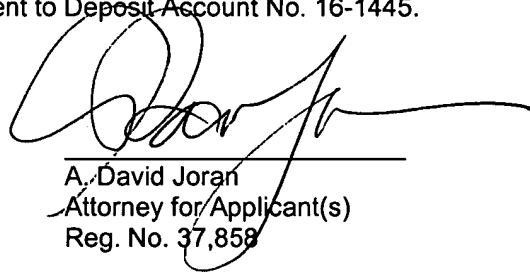
Without prejudice and in the interests of facilitating prosecution, applicants have amended claim 1 to recite: "an agent that slows or arrests Alzheimer's disease selected from a cognition enhancer" by insertion of the underlined terms.

Applicants submit that currently amended claim 1 and claims 8, 10, 15-23 and 25-35 are patentable under 35 USC § 112, second paragraph, and respectfully request the Examiner to withdraw the rejection.

In view of the amendments set forth herein and remarks above, the applicants respectfully submit that the pending claims are fully allowable, and solicit the issuance of a notice to such effect. If a telephone interview is deemed to be helpful to expedite the prosecution of the subject application, the Examiner is invited to contact applicants' undersigned attorney at the telephone number provided.

The Commissioner is hereby authorized to charge any fees required under 37 C.F.R. §§ 1.16 and 1.17 or to credit any overpayment to Deposit Account No. 16-1445.

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